Citation:

Welty FK, Lee KS, Lew NS, Zhou JR. Effect of soy nuts on blood pressure and lipid levels in hypertensive, prehypertensive, and normotensive postmenopausal women. *Arch Intern Med*. 2007 May 28;167(10):1060-7.

PubMed ID: 17533209

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study targeting postmenopausal women was to determine the effects of soy nuts on blood pressure, lipid levels, and glucose.

Inclusion Criteria:

- Absence of menses for at least 12 months
- Irregular periods and hot flashes

Exclusion Criteria:

- Current cigarette smoking or smoking in the previous year
- Clinical coronary artery disease, peripheral artery disease, or cerebrovascular disease
- Known diabetes mellitus or a fasting glucose level of 126 mg/dL or greater (7.0 mmol/L)
- History of breast cancer
- Fasting triglyceride level greater than 400 mg/dL (>4.52 mmol/L)
- Systolic BP of 165 mm Hg or greater or diastolic BP of 100 mm Hg or greater
- Untreated hypothyroidism
- Systemic or endocrine disease known to affect lipid, mineral, or bone metabolism
- Consumption of more than 21 alcoholic drinks per week
- Use of lipid-lowering drugs, hormone therapy, medications for osteoporosis, and soy products was discontinued for 2 months before entering the study
- Participants took a multivitamin but no additional vitamin or mineral supplements or other soy products during the study

Description of Study Protocol:

Recruitment: Methods not described

Design Randomized controlled crossover trial

Blinding used (if applicable): none

Intervention (if applicable):

- Participants were instructed by a registered dietitian to consume a Therapeutic Lifestyle Change (TLC) diet.
- After a 4-week run-in, compliant participants were randomized in a crossover design between 2 diet sequences for 8-week periods including the TLC diet without soy or the TLC with pre-packaged daily allowances of one-half cup of unsalted soy nuts.
- After a 4-week washout on the TLC diet alone, participants crossed over to the other arm for an additional 8 weeks.
- The Therapeutic Lifestyle Change (TLC) diet is recommended by the Adult Treatment Panel of the National Cholesterol Education Program and consists of 30% energy from total fat (<7% saturated fat, 12% monounsaturated fat, and 11% polyunsaturated fat), 15% from protein, and 55% from carbohydrate, less than 200 mg cholesterol per day, 1200 mg of calcium and 2 fatty fish meals per week.
- Soy nut diet included pre-packaged daily allowances of one-half cup of unsalted soy nuts containing 25 g of soy protein and 101 mg of aglycone isoflavones, divided into 3 or 4 portions spaced throughout the day

Statistical Analysis:

- Continuous variables were compared using 2-tailed paired (within BP group) and unpaired (normotensive to hypertensive) t tests.
- To examine carryover effect, a repeated-measures ANOVA with order and treatment as independent variables and outcome as the dependent variable was performed.
- Pearson correlation coefficients were also used to assess relationships between continuous variables.

Data Collection Summary:

Timing of Measurements

Measurements made before and after each diet period.

Dependent Variables

- Blood pressure: performed using standardized procedures and the cycling Dinamps
- Lipid and apolipoprotein B measurement: collected, assessed, and analyzed using a Lipid Standardization Program

Independent Variables

- TLC diet without soy or the TLC with pre-packaged daily allowances of one-half cup of unsalted soy nuts.
- Diet: Assessed from 3 sets of 3-day food records for each diet arm using Nutritionist V, version 3.0

Control Variables

- Exercise: recorded the number of minutes of exercise performed daily throughout the study

Description of Actual Data Sample:

Initial N: assumed 60 women; the number of subjects initially recruited to the run-in diet is not reported.

Attrition (final N): Normotensive women (n=48); Hypertensive women (n=12)

Age: Normotensive women (53.5 years, SD 5.3), Hypertensive women (58.3 years, SD 6.5); p=0.01

Ethnicity: not reported

Other relevant demographics

Anthropometrics

Hypertensive women were significantly older, heavier, and had high total cholesterol, LDL-C, and apoB levels than normotensive women:

- BMI: Normotensive women (25.4, SD 4.9), Hypertensive women (28.0 years, SD 1.3); p=0.008
- Total Chol: Normotensive women (228 mg/dL, SD 39), Hypertensive women (248 mg/dL, SD 62); p=0.01
- LDL-C: Normotensive women (143 mg/dL, SD 32), Hypertensive women (164 mg/dL, SD 57); p=0.01
- apoB: Normotensive women (111 mg/dL, SD 19), Hypertensive women (126, SD 37); p=0.01

Location: United States

Summary of Results:

Key Findings

- Compared with the TLC diet alone, the TLC diet plus soy nuts lowered systolic and diastolic blood pressure by 9.9% and 6.8%, respectively, in hypertensive women (systolic blood pressure >140 mmHg) and 5.2% and 2.9% respectively, in normotensive women (systolic blood pressure <120 mmHg).
- Further subdivision of normotensive women revealed that systolic and diastolic blood pressures were lowered 5.5% and 2.7%, respectively, in prehypertensive women (systolic blood pressure 120 - 139 mmHg) and 4.5% and 3.0%, respectively, in normotensive women.
- Soy nut supplementation lowered LDL cholesterol and apolipoprotein B levels by 11% and 8% (P = 0.04 for both), respectively, in hypertensive women but had no effect in normotensive women.
- No changes in total cholesterol, HDL-c, or triglycerides were observed in any group.

Diet compliance

- Urinary isoflavone levels were higher in the soy diet arm compared to the control arm
- Among normotensive women, when compared to the control diet the soy diet was significantly higher in kilocalories, polyunsaturated fat, and protein; and lower in total fat, saturated fat, carbohydrates
- Among hypertensive, when compared to the control diet the soy diet was significantly higher in kilocalories; and lower in total fat and saturated fat
- Additional results on calcium and cholesterol suggest that the study participants were compliant with the TLC diet

Blood pressure, BMI, Lipid, and Glucose Results at the End of Each Diet Period in Normotensive and Hypertensive Women, *expressed in means (SD)*

	Normotensive Women (n=48)			Hypertensive Women (n=12)		
Variables	Control Diet	Soy Diet	P value	Control Diet	Soy Diet	P value
Systolic BP, mmHG	110 (7)	105 (8)	0.003	152 (12)	137 (15)	0.003
Diastolic BP, mm Hg	67 (7)	65 (7)	0.06	88 (7)	82 (8)	0.001
BMI	24.9 (4.7)	25.0 (4.6)	0.21	28.0 (4.3)	27.7 (4.3)	0.14
Total-C, mg/dL	228 (39)	224 (36)	0.28	248 (62)	230 (45)	0.08
LDL-C, mg/dL	143 (32)	142 (31)	0.55	164 (57)	146 (46)	0.04
HDL-C, mg/dL	58 (15)	59 (14)	0.21	56 (10)	56 (10)	0.73
Triglycerides, mg/dL	128 (97)	119 (83)	0.31	128 (74)	114 (50)	0.29
Apolipoprotein B, mg/dL	111 (19)	108 (24)	0.25	126 (37)	116 (32)	0.04
Glucose, mg/dL	98 (10)	97 (9)	0.30	97 (11)	95 (12)	0.27

- Order of diets did not affect responses
- Soy nut supplementation significantly reduced SBP and DBP in all 12 hypertensive women and in 40 of 48 normotensive women
- There was no change for BMI or exercise on the soy diet versus the control diet, therefore, neither weight change nor exercise level accounts for the lower BP

Other Findings

- In the 8 hypertensive women with LDL-C levels greater than 140 mg/dL, the percentage reduction in SBP was positively correlated with the level of equol in the soy diet arm
- When normotensive women were further subdivided into prehypertensive and normotensive women, both groups had significant reductions in SBP, and there was a trend toward reduction in DBP in the soy diet arm compared with the control diet arm

Author Conclusion:

In conclusion, soy nuts significantly lowered systolic and diastolic blood pressure in normotensive and hypertensive postmenopausal women and lowered levels of LDL-cholesterol and apoB in hypertensive, hyperlipidemic women. This study was performed in the free-living state; therefore, dietary soy may be a practical, safe and inexpensive modality to reduce blood pressure. If the findings are repeated in a larger group, they may have important implications for reducing cardiovascular risk in postmenopausal women on a population basis.

Reviewer Comments:

Only 12 women in the hypertensive group. Despite significant differences among normotensive and hypertensive women as baseline, no attempt was made to account for these differences in the analyses.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	No

3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	No
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	N/A
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	N/A
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A

6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes

	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes